



## **Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States**

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## Introduction (Last updated December 24, 2019; last reviewed December 24, 2019)

Recommendations regarding HIV screening in pregnancy, treatment of pregnant women who are living with HIV, and the use of antiretroviral (ARV) drugs to prevent perinatal transmission of HIV have evolved considerably in the United States since the mid-1990s, reflecting changes in both the epidemic and the science of prevention and treatment. Current recommendations for universal prenatal HIV counseling and testing, antiretroviral therapy (ART) for all pregnant women with HIV, scheduled cesarean delivery for women with plasma HIV RNA >1,000 copies/mL near delivery, appropriate infant ARV management, and avoidance of breastfeeding have resulted in a dramatic decrease in the rate of perinatal transmission of HIV to 1% or less in the United States and Europe.<sup>1</sup> In 2016, only 44 infants were born with HIV infection in the United States; the estimated incidence of perinatally acquired HIV infection was 1.1 out of 100,000 live births.<sup>2</sup>

In response to this success, the Centers for Disease Control and Prevention has developed a goal of eliminating perinatal HIV transmission in the United States, defined as reducing perinatal transmission to an incidence of <1 infection per 100,000 live births and to a rate of <1% among HIV-exposed infants.<sup>3</sup> However, incomplete implementation of routine antenatal HIV testing and other recommended interventions remains a barrier to achieving this goal.<sup>4,5</sup> Laws that promote universal HIV testing for pregnant women vary by jurisdiction, and prenatal testing coverage is higher in states with stronger regulations for testing all pregnant women.<sup>6,7</sup> Testing coverage is also poorer for pregnant women in subgroups that are perceived by health care providers to be at low risk of HIV acquisition (e.g., women who are married, white, non-Hispanic, or multiparous).<sup>8</sup> To address such challenges, many states and the District of Columbia have developed additional effective strategies to advance progress towards eliminating perinatal HIV transmission.<sup>9</sup>

Approximately 5,000 women with HIV give birth annually in the United States.<sup>10</sup> In addition to primary prevention of HIV infection in women, the best way to prevent HIV infection in infants is to focus on appropriate overall medical care for women with HIV; this includes comprehensive reproductive health care, family planning and preconception care services, optimization of HIV treatment, and maintenance of care between pregnancies. A critical component of preventing perinatal HIV transmission is ensuring that a woman receives ART that maximally suppresses viral replication as early as possible during pregnancy or, ideally, prior to conception.

A critical role of the Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission (the Panel) is to evaluate the many ARV drugs that are available for adults and assess the risks and benefits of using these drugs in pregnant women. The Office of AIDS Research Advisory Committee (OARAC)-sponsored Panel on Antiretroviral Guidelines for Adults and Adolescents primarily considers efficacy and safety evidence when making recommendations for ART regimens. Secondary considerations include characteristics that help promote adherence, such as improved tolerability or convenience (e.g., whether a regimen is available as a fixed-dose combination with once daily dosing). When considering which ARV drugs to recommend for use in pregnant women (or women who may become pregnant), the Panel generally uses data from efficacy studies performed in nonpregnant adults; however, because drug exposure can change during pregnancy, data from direct pharmacokinetic (PK) studies in pregnant women are required.

In addition to considering direct evidence about short-term safety in pregnant women, the Panel must also make judgments about fetal safety. The Panel makes an initial assessment based on data from preclinical animal studies, analyses of reports to the [Antiretroviral Pregnancy Registry](#), and all available post-marketing surveillance data.

When there is strong evidence of fetal (or maternal) harm or unacceptable drug exposure, it is straightforward for the Panel to make recommendations against the use of a specific drug; however, this situation is unusual. More often, the Panel must make recommendations for ARV drugs for which there are insufficient PK data in pregnant women and/or inadequate safety information on fetal exposure early in pregnancy or during the periconception period. Policymakers, regulators, clinicians, and community advocates are striving to improve the availability of data on ARV drug exposure and safety in women who are pregnant or breastfeeding, or in

women who are of reproductive potential.<sup>11-13</sup>

In the meantime, to ensure that pregnant women are not denied the best available ART regimens—while acknowledging that some drugs have not yet been sufficiently evaluated for evidence of fetal or maternal harm—the Panel uses a graded approach to making recommendations for regimens to use during pregnancy:

- ART regimens that are designated as *Preferred* in pregnancy are those that have been shown to be effective and durable in clinical trials in adults. *Preferred* regimens have acceptable toxicity and ease of use, pregnancy-specific PK data to guide dosing, and available data suggest a favorable risk-benefit balance compared to other ARV options, incorporating outcomes for women, fetuses, or newborns. Some *Preferred* drugs may have minimal toxicity or teratogenicity risks that are offset by other advantages for women with HIV who are pregnant or who are trying to conceive.
- Preferred ART regimens for nonpregnant adults that do not meet the above criteria can be considered as options for *Alternative* regimens in pregnant women when available data on the use of these regimens in pregnancy are generally favorable but limited. Most *Alternative* drugs or regimens are associated with more PK, dosing, tolerability, formulation, administration, or interaction concerns than those in the preferred category, but they are acceptable for use in pregnancy. They may also have known toxicity or teratogenicity risks that are offset by other advantages for women with HIV who are pregnant or who are trying to conceive.
- Use caution when considering the use of regimens that contain drugs with little or no pregnancy data. These regimens are considered to have *Insufficient Data to Recommend* for initiation in pregnancy, but there are no specific data that would support a recommendation to discontinue these regimens in women who become pregnant while taking them.
- Some drugs are designated as *Not Recommended Except in Special Circumstances* because the Panel recognizes that there may be situations in which treatment-experienced pregnant women may need to initiate or continue drugs with limited safety and efficacy data or specific safety concerns to reach or maintain viral suppression.
- Some drugs are designated as *Not Recommended* in pregnancy because they have inferior virologic efficacy, because PK data demonstrates low drug levels and a risk of viral rebound during pregnancy, or because they are associated with potentially serious maternal or fetal safety concerns.

The Panel systematically reviews all new information from the Antiretroviral Pregnancy Registry, published studies, and other sources to update their drug recommendations. The Panel also coordinates with the Panel on Antiretroviral Guidelines for Adults and Adolescents when there are concerns related to drug safety in pregnancy.

These guidelines update the December 2018 *Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States*. The Panel, a working group of the National Institutes of Health (NIH) OARAC, develops these guidelines. The Panel collaborates with the companion NIH OARAC Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV to jointly develop recommendations in overlapping areas (e.g., [Maternal HIV Testing and Identification of Perinatal HIV Exposure](#), [Diagnosis of HIV Infection in Infants and Children](#), [Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection](#)), as well as to ensure general harmony between the guidelines. Health care providers should discuss the information in these guidelines with pregnant women who are living with HIV in order to make collaborative, informed decision-making regarding the use of ARV drugs during pregnancy, the use of scheduled cesarean delivery to reduce the risk of perinatal transmission of HIV, and decision-making around the use of ARV drugs in infants who have been exposed to HIV. The recommendations in these guidelines are accompanied by discussions of common circumstances that occur in clinical practice and the factors that influence treatment considerations. The Panel recognizes that strategies to prevent perinatal transmission and

concepts related to managing HIV in pregnant women are rapidly evolving, and the Panel will continue to consider new evidence and adjust recommendations accordingly. The current guidelines are available on the [AIDSinfo website](#). The National Perinatal HIV Hotline (1-888-448-8765) is a federally funded service that provides free clinical consultation to providers caring for women who are living with HIV or who are at risk for HIV and their children, and it serves as a resource for obtaining expert consultation on individual cases.

The Panel's recommendations are designed to ensure that women receive the full benefit of ART for their own health and to prevent perinatal transmission. However, the Panel recognizes that women have the right to make informed choices about treatment during pregnancy, even when their choices differ from a health care provider's recommendations.

The current guidelines have been structured to reflect the management of an individual mother-infant pair and are organized into a brief discussion of preconception care followed by principles for managing the care of a woman and her infant during the antepartum, intrapartum, and postpartum periods. Although perinatal transmission of HIV occurs worldwide, these recommendations have been developed for use in the United States. Alternative strategies may be appropriate in other countries (see the [World Health Organization guidelines](#) for more information).

## Guidelines Development Process

**Table 1. Outline of the Guidelines Development Process** (page 1 of 2)

Topic	Comment
<b>Goal of the Guidelines</b>	Provide guidance to HIV care practitioners in the United States on the optimal use of antiretroviral (ARV) agents to treat HIV infection in pregnant women and to prevent perinatal HIV transmission in HIV-exposed infants.
<b>Panel Members</b>	<p>The Panel is composed of approximately 30 voting members who have expertise in managing the care of pregnant women with HIV (e.g., training in obstetrics/gynecology, infectious diseases, or women's health), pharmacology of ARV drugs during pregnancy, and interventions for prevention of perinatal transmission (e.g., specialized training in pediatric HIV infection). The Panel also includes community representatives with knowledge of HIV infection in pregnant women and interventions for prevention of perinatal transmission.</p> <p>The U.S. government representatives, appointed by their agencies, include at least one representative from each of the following Department of Health and Human Services agencies: the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Health Resources and Services Administration (HRSA), and the National Institutes of Health (NIH). Members who do not represent U.S. government agencies are selected by Panel members after an open call for nominations. Each member serves on the Panel for a 3-year period, with an option for re-appointment. The Panel may also include liaison members from the National Perinatal HIV Hotline, the American Academy of Pediatrics' Committee on Pediatric AIDS, and the American College of Obstetricians and Gynecologists. A list of all Panel members can be found in the <a href="#">Guidelines Panel Members</a> section.</p>
<b>Financial Disclosures</b>	All members of the Panel submit an annual written financial disclosure that reports any association with manufacturers of ARV drugs or diagnostics used to manage HIV infection. See <a href="#">Financial Disclosure</a> for a list of the latest disclosures.
<b>Users of the Guidelines</b>	Providers of care to pregnant women with HIV and to infants who have been exposed to HIV
<b>Developer</b>	The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission—a working group of the Office of AIDS Research Advisory Council (OARAC)
<b>Funding Source</b>	Office of AIDS Research, NIH
<b>Evidence for Recommendations</b>	The recommendations in these guidelines are generally based on studies published in peer-reviewed journals. On some occasions, particularly when new information may affect patient safety, unpublished data that was presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
<b>Recommendation Grading</b>	See <a href="#">Table 2</a> .

## Guidelines Development Process

**Table 1. Outline of the Guidelines Development Process** (page 2 of 2)

Topic	Comment
<b>Method of Synthesizing Data</b>	Each section of the guidelines is assigned to a small group of Panel members with expertise in the area of interest. A structured literature search is conducted by a technical assistance consultant and provided to the Panel working group. The members review and synthesize the available data and propose recommendations to the entire Panel. The Panel discusses all proposals during monthly teleconferences. Proposals are modified based on Panel discussions and then distributed, with ballots, to all Panel members. If there are substantive comments or votes against approval, the recommended changes and areas of disagreement are brought back to the full Panel (via email or teleconference) for review, discussion, and further modification to reach a final version that is acceptable to all Panel members. The recommendations in these final versions represent consensus of Panel members and are included in the guidelines as official Panel recommendations.
<b>Other Guidelines</b>	These guidelines focus on pregnant women with HIV and their infants. Other guidelines (all of which are available on the <a href="#">AIDSinfo website</a> ) outline the use of ARV agents in nonpregnant adults and adolescents with HIV; use of ARV agents in infants and children with HIV; treatment and prevention of opportunistic infections (OIs) in adults and adolescents with HIV, including pregnant women; treatment and prevention of OIs in children who have been exposed to HIV or who have HIV infection; and treatment of people who experience occupational or nonoccupational exposure to HIV. Preconception management for nonpregnant women of reproductive potential is briefly discussed in this document. However, for a more detailed discussion of the issues surrounding the treatment of nonpregnant adults, please consult the <a href="#">Adult and Adolescent Antiretroviral Guidelines</a> and the <a href="#">Adult and Adolescent Opportunistic Infection Guidelines</a> .
<b>Update Plan</b>	The Panel meets monthly by teleconference to review data that may affect the content of the guidelines. Updates may be prompted by new drug approvals (or new indications, new dosing formulations, and/or changes in dosing frequency), significant new safety or efficacy data, or other information that may have a significant impact on the clinical care of patients. In the event of significant new data that may affect patient safety, the Panel may issue a warning announcement and recommendations on the <a href="#">AIDSinfo website</a> until the guidelines can be updated with appropriate changes.
<b>Public Comments</b>	A 2-week public comment period follows the release of the updated guidelines on the <a href="#">AIDSinfo website</a> . The Panel reviews comments to determine whether additional revisions to the guidelines are indicated. The public may also submit comments to the Panel at any time at <a href="mailto:contactus@aidsinfo.nih.gov">contactus@aidsinfo.nih.gov</a> .

## Basis for Recommendations

The recommendations in these guidelines are based on scientific evidence and expert opinion. Each recommendation statement includes a letter (**A**, **B**, or **C**) that represents the strength of the recommendation and a Roman numeral (**I**, **II**, or **III**) that represents the quality of the evidence that supports the recommendation.

**Table 2. Rating Scheme for Recommendations**

Strength of Recommendation	Quality of Evidence for Recommendation
<b>A:</b> Strong recommendation for the statement	<b>I:</b> One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
<b>B:</b> Moderate recommendation for the statement	<b>II:</b> One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
<b>C:</b> Optional recommendation for the statement	<b>III:</b> Expert opinion

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